REMARKS

Reconsideration is respectfully requested. Claims 1, 4, 5, 7, 10, 11, 13, 17, and 19-24 are pending. New claim 24 is added. Claims 2, 3, 6, 8, 9, 12, 14-16, and 18 are canceled. Claims 17 and 19-23 are withdrawn. No new matters have been added due to the amendments. Amendment to and cancellation of the claims does not affect inventorship.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Finality of Restriction

In the previous response, Applicants had elected Group I (claims 1-16) with traverse, and amended claims 17-23 of Group II to depend from claims within elected group. In the instant Office Action, the Examiner has made the restriction final. Applicants respectfully traverse on the grounds that the basis for restriction pursuant to M.P.E.P. §803 has not been met.

An application may properly be required to be restricted to one of two or more claimed inventions **only if:**

1. the inventions are independent or distinct as claimed; **and**

2. the search and examination of the entire application places a serious burden on the examiner. M.P.E.P. §803.

Restriction is only proper when both conditions are satisfied.

A. Claims In Groups I And II Are Not "Independent" Inventions

As outlined in M.P.E.P. §802.01(I),

> The term "independent" (i.e., not dependent) means that there is no disclosed relationship between the two or more invention claimed, that is, they are

> unconnected in design, operation, and effect. For example, a process and an apparatus **incapable** of being used to practice the process are independent inventions. (Emphasis added).

The Applicants submit that the inventions are not "independent", as they are not "unconnected in design, operation, and effect." In fact, they have the same design, operation and effect.

In the present invention, the claims of Group II are dependent from the claims of group I, thus there is a clear relationship between claims of the two groups. Furthermore, if the claim 13 of Group I proves to be novel upon examination, the claims of Group II will be novel as well. Applicants therefore submit that the current restriction is not proper and should be withdrawn.

B. Claims In Groups I and II Are Not "Distinct" Inventions

The Examiner's attention is respectfully drawn to M.P.E.P. §806.05(j), which states that

> To support a requirement for restriction between two or more related product invention, or between two ore more related process invention, both two-way distinctness and reasons for insisting on restriction are necessary, i.e. separate classification, status in the art, or field of search. See M.P.E.P. §808.02.

M.P.E.P. §806.05(j) goes on to outline the three requirements under related inventions:

> . . . the inventions are distinct if
>
> (A) the inventions as claimed do not overlap in scope, i.e., are mutually exclusive;
>
> (B) the inventions as claimed are not obvious variants; and
>
> (C) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 802.01.
>
> The burden is on the examiner to provide an example to support the determination that the inventions are distinct, but the example need not be documented. If applicant either proves or provides convincing evidence that the example suggested by the examiner is not workable, the burden is on the examiner to suggest another viable example or withdraw the restriction requirement.

The Applicants submit that the claims in Groups I and II do not display either two-way distinctness or a reason for insisting on restriction. As to the former, at a

minimum, the inventions do not have a materially different design, mode of operation, function, or effect. As to the latter, claims of Group II are dependent from the claim of Group I. As such, the claims do not have separate classification, status in the art, or field of search.

C. The Search and Examination of All Claims Is Not "Undue"

The Examiner's attention is respectfully drawn to M.P.E.P. §808.02:

> Where the related inventions as claimed are shown to be independent or distinct under the criteria of MPEP § 806.05(c) - § 806.06, the examiner, in order to establish reasons for insisting upon restriction, must explain why there would be a serious burden on the examiner if restriction is not required. Thus the examiner must show by appropriate explanation one of the following:
>
> (A) **Separate classification thereof:** This shows that each invention has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Patents need not be cited to show separate classification.
>
> (B) **A separate status in the art when they are classifiable together**: Even though they are classified together, each invention can be shown to have formed a separate subject for inventive effort when the examiner can show a recognition of separate inventive effort by inventors. Separate status in the art may be shown by citing patents which are evidence of such separate status, and also of a separate field of search.
>
> (C) **A different field of search:** Where it is necessary to search for one of the inventions in a manner that is not likely to result in finding art pertinent to the other invention(s) (e.g., searching different classes/subclasses or electronic resources, or employing different search queries, a different field of search is shown, even though the two are classified together. The indicated different field of search must in fact be pertinent to the type of subject matter covered by the claims. Patents need not be cited to show different fields of search.
>
> Where, however, the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among independent or related inventions.

As the claims in Group II depend from the claim in Group I and thus are in the identical class and subclass, explanation (A) has not been met.

Applicants also submit that the search associated with the examination of Group I is the same search that would be required if the Examiner were to search claims of Group II. Accordingly, if the inventions claimed in Group I prove to be novel, no additional search by the Examiner will be needed. In that instance, there is no further search burden imposed upon the Examiner to also examine claims of Group II.

Thus, the Applicants submit that the search and examination of all the groups would not be "undue".

In light of the foregoing, the claims of Groups I and II are not independent and have not achieved separate classification, a separate status in the art, or a different field of search. Accordingly, examination of the entire application does not place a serious burden on the examiner and the restriction requirement should be withdrawn.

Claim Amendment

Claims 1, and 7 are amended for technical clarity. Claim 5 is amended. Support is found, for example, in original claim 6. Claims 11 and 19 are amended. Support is found, for example, in original claim 12. New claim 24 is added. Support is found, for example, in original claims 1, 5, and 6.

In the Specification

Title

The title is objected to as being no descriptive. The title is amended. As such, Applicants respectfully request the rejection be withdrawn.

Abstract

The abstract is objected to because it does not describe the claimed invention. Without acquiescing to the propriety of the rejection, the abstract is amended. As such, Applicants respectfully request the rejection be withdrawn.

The Specification

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. The specification is amended to remove the hyperlinks. As such, Applicants respectfully request the rejection be withdrawn.

The specification is objected to for informalities: (a) the use of pSX26; and (b) the abbreviations of "TCEP" and "IMAC" in paragraph [00179].

Applicants respectfully submit that the pSX26 vector is a proprietary vector engineered for Syrrx, Inc. (now Takeda San Diego, Inc.) by Invitrogen; it is not commercially available.

The specification is amended to correct the informalities related to the abbreviations of "TCEP" and "IMAC" in paragraph [00179]. As such, Applicants respectfully request the objection be withdrawn.

The specification is objected for failure to comply with the requirement of 37 CFR 1.821(a)1(1) and (a)(2) with regard to sequence identifier in the specification. The specification is amended to include sequence identifiers. As such, the application complies with the requirement of 37 CFR 1.821(a)1(1) and (a)(2) and Applicants respectfully request the rejection be withdrawn.

Claims Rejections - 35 U.S.C. § 112, First Paragraph

I. Written Description

Claims 1, 4-7, 10-13, and 16 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Applicants respectfully traverse.

Claims 6, 12, and 16 have been canceled, rendering the rejections moot.

A. The application meets the written description requirement because the application discloses enough to convince a person of skill in the art that the inventor possessed the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. M.P.E.P. § 2163.

The instant application discloses that Applicants have conducted systematic screening to test numerous crystallization conditions and have produced numerous MvaS crystals:

> [S]ystematic broad screen crystallization trials were performed on an MvaS complex using the sitting drop technique. In each experiment, a 100nL mixture of MvaS complex and precipitant was placed on a platform positioned over a well containing 100μL of the precipitating solution. Precipitate and crystal formation was detected in the sitting drops. Fine screening was then carried out for those crystallization conditions that appeared to produce precipitate and/or crystal in the drops.
> Based on the crystallization experiments that were performed, a thorough understanding of how different crystallization conditions affect MvaS crystallization was obtained. Based on this understanding, a series of crystallization conditions were identified that may be used to form crystals comprising MvaS. These conditions are summarized in Table 5.
> Paragraphs [0090] and [0091].

Thus, the instant application not only describes methods to obtain claimed crystals and a series of crystallization conditions as shown in Table 5 in page 20, but also describes numerous crystals obtained under those conditions. Out of these numerous crystals, the inventors picked one condition to pursue; clearly, the inventors made a wide variety of crystals under a variety of conditions. The chosen crystal is described in detail in Example 2. The instant application further discloses additional crystals could be produced used the disclosed methods and conditions:

> [V]ariations on the crystallization conditions described herein can be readily determined by taking the conditions provided in Table 5 and performing fine screens around those conditions by varying the type and concentration of the components in order to determine additional suitable conditions for crystallizing MvaS, variants of MvaS, and ligand complexes thereof.
> Paragraph [0092].

The Examiner appears to suggest that the written description requirement requires the explicit disclosure of a number of different species. However, the Examiner's attention is respectfully drawn to a recent Federal Circuit written description case, *Faulkner v. Inglis*, 79 USPQ2d 1001 (Fed. Cir. 2006), which reiterated the standard for written description and enablement requirement:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation. *Id.* at 1007.

Specifically, the Court held that:

> (1) [E]xamples are not necessary to support the adequacy of a written description, (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involved a biological macromolecule must contain a recitation of known structure.

Even if only a single crystal was described, there may be situations where one species adequately supports a genus. See, e.g., *In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 232, 326-27 (CCPA 1981). M.P.E.P. § 2163.

Here, the Applicants present methods and numerous conditions to obtain the claimed crystals as well as numerous crystals produced using claimed methods. In view of the science and the teaching in the specification, Applicants submit that the instant application provides

sufficient disclosure such that a person of skill in the art knows that the inventor possessed the invention including sufficient variations of the disclosed species to support the presently claimed genus. The Applicants further submit that a person of skill in the art of producing protein crystals would be well versed in using the claimed methods to produce claimed crystals under the guidance of the instant application, and Faulkner dictates a finding of adequate written description.

B. The application is sufficient to that show the applicant was in possession of the claimed genus because the claimed subject matter is defined structurally.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). M.P.E.P. § 2163.

The claims presented structurally require that the protein "consists of SEQ ID NO:1." Moreover, claims 5 and 11 further require the protein crystal "has a crystal lattice in a $P2_12_12_1$ space group and unit cell dimensions, +/- 5%, of a=68.7 b=79.6 c=150.2, $\alpha=\beta=\gamma=90$."

Since the claimed subject matter is defined structurally, and in view of the guidance provided in the application that discussed more fully below, the instant application is sufficient to show the applicant was in possession of the claimed genus.

In conclusion, the claimed invention provides sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed scope of crystals. As such, the rejection based on this ground is improper and should be withdrawn.

II. Enablement

Claims 1, 4-7, 10-13, and 16 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. Specifically, the Examiner alleges that the specification fails to enable all crystals and methods as broadly encompassed by the claims. Applicants respectfully traverse.

Claims 6, 12 and 16 have been canceled, rendering the rejections moot.

The enablement requirement is met if the description enables any mode of making and using the invention. Moreover, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *Johns Hopkins Univ. v. Cellpro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998) (citations omitted). Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. M.P.E.P. § 2164.01.

As argued above, the specification discloses a variety of crystals, formed under a variety of conditions. The fact that the inventor's chose only one of the crystals to move forward for further analysis, does not negate the existence of the other crystals. Accordingly, Applicants argue the enablement requirement is met.

In addition, as outlined above, a person of skill in the art of producing crystals would be well versed in using the claimed methods to produce claimed crystals under the guidance of the instant application. Applicants also point out that there is no need to test different conditions to obtain the optimal parameters in order to produce new crystals within the scope of the claim. Instead, generating additional crystals is well within the ability of one of skill in the art purely

through using the disclosed methods as the instant application discloses a range of conditions for growing crystals. For example, the instant application discloses that:

> Crystals comprising MvaS may be formed by a variety of different methods known in the art. For example, crystallizations may be performed by batch, dialysis, and vapor diffusion (sitting drop and hanging drop) methods. A detailed description of basic protein crystallization setups may be found in McRee, D. and David. P., Practical Protein Crystallography, 2nd Ed. (1999), Academic Press Inc. Further descriptions regarding performing crystallization experiments are provided in Stevens, et al. (2000) Curr. Opin. Struct. Biol.: 10(5):558-63, and U.S. Patent Nos. 6,296,673, 5,419,278, and 5,096, 676.
> Paragraph [0087].

Given the absence of the need to perform any further screening to obtain optimal conditions for crystal growing, no undue experimentation is required to enable one of ordinary skill in the art to enjoy the fullest scope of the claimed invention. The Examiner's attention is again respectfully drawn to the *Falkner* case, in which the Federal Circuit held that "[a] claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. "

Accordingly, Applicants submit that the instant application reasonably provides enablement for making the crystals as encompassed by the claims. As such, the rejection based on this ground is improper and should be withdrawn.

Claim Rejection- 35 U.S.C. § 103

Claim 16 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Paulsen et al., (Science 2003, 299, 2071-2074) ("*Paulsen*") in view of EMBL accession number Q835L4, Wilding et al., (J. Bacteriol. 2000, 182, 4319 –4327) ("*Wilding*") and Ford et la., (Protein Expr. Puri. 1991, 2, 95-107) ("*Ford*").

Claim 16 is canceled, rendering the rejection moot.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1000.

Respectfully submitted,

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